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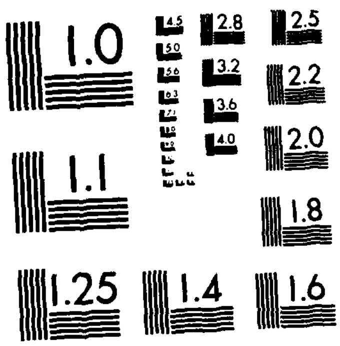
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A background section describes the neuromagnetic method and its history to date. The Technical Report section describes the post year's accomplishments, including a thorough study of effects of selective attention during a dichotic listening task. There were an elevation of N1 and P2 (using a quasi-steady state stimulus). The N1 and P2 sources could not be distinguished from those obtained using a transient stimulus paradigm. The fields associated with these sources increase in intensity during attention. This is not due to the activity of sources recruited during attention, but to modulated activity of neurons in or near primary auditory cortex. This is consitent with a Triesman-like filter theory of attention. Also, physical parameters of stimulation, e.g., loudness, have little or no effect. However, the effect is sharply diminished when both stimuli are presented to both ears with equal loudness. A collaboration with other investigators is planned to compare our results with results obtained in a more conventional manner. A new method for obtaining graded levels of attention is described. A visual experi- (OVER)

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BLOCK 19 Abstract

ment is underway, and is giving us similar results. A single-position method for determining the location, orientation and strength of the dipole source is described. This method will be applied to a P300 study, which will follow-up an odd-ball study just completed. The latter gave results similar to those obtained previously, but the method is insufficiently insensitive to determine if changing P300 latency is due to a change in source. The planned experiment should make this possible.

AFOSR-TR- 86-0417

INTERIM SCIENTIFIC REPORT

PERCEPTUAL FACTORS IN WORKLOAD: NEUROMAGNETIC STUDIES

by L. Kaufman and S. J. Williamson

New York University

BACKGROUND

This report describes the work accomplished on our AFOSR contract No. F49620-85-K-0004 during the period 01/01/85 to 12/31/85. However, before reporting on our results, we will present the following general description of neuromagnetism and its relation to other techniques for studying the structure and functioning of the brain. This background information is intended for readers who are unfamiliar with the relatively new methods we are employing on this project.

The introduction of computerized axial tomography (CT scan) and of magnetic resonance imaging (MRI) has revolutionized medical practice as well as basic research in the neurosciences. It is now possible to see detailed anatomical structures with a clarity that was unattainable previously. The advent of positron emission tomography (PET scan) provides us with a potentially powerful research tool for studying the ways in which functions of the brain vary with different kinds of mental activity. PET scan depends upon the detection of gamma rays emitted when

positrons associated with a radioactive analogue to glucose are anihilated. This glucose-analogue is taken up from the blood stream in greater or lesser amounts by active nerve cells, and the emitted gamma rays reflect differential amounts of activity.

Another way to study differential neural activity in the human brain is by measuring the spontaneous electroencephalogram (EEG), and the event related potential (ERP). Such measures are made in many laboratories while human subjects are engaged in performing various tasks, and the measures do vary with the nature of the task and the demands placed on the subject. In typical experiments different components of the ERP are affected differentially by whether or not attention is being paid to a particular stimulus, if an event is or is not anticipated, and so on. (In this report we define component as a salient deflection in the waveform of the ERP, and each component is given a name that is consistent with existing conventions.) Recent work by Gevins (1985) indicates that it is possible to identify the regions of the cerebral cortex that become active during the performance of such tasks, and to determine how the pattern of activity among these regions varies with the nature of the task. This requires the use of a large number of recording electrodes and extremely sophisticated means for analyzing the measured potential differences, as well as a realistic physical model of the subject's head. Gevins relies on

MRI techniques in generating his models. By contrast, most work employing the EEG and ERP involves the use of relatively few electrodes, and investigators rely instead on the functional relationship between parameters of the task and the concomitant changes in particular components. In fact, the bulk of the vast ERP literature may be aptly described as being <u>phenomenological</u> in orientation.

Despite the emphasis on phenomenology, the ERP literature is filled with questions as to the origins of specific components. Different methods have been used to answer these questions. One involves modelling the head as three concentric spheres of different conductivity, and the observed potentials are mapped onto the surface of the outer sphere. The investigator then places a <u>current dipole</u> within the central sphere and computes the pattern of potentials that this imaginary source produces on the outer surface. This computed pattern is then made to match the observed pattern by changing the strength (moment), position and orientation of the current dipole within the central sphere. When an "acceptable" match is achieved, it is assumed that the source is in a corresponding position within the subject's head (Darcey, et al. 1980; also see Nunez, 1981, for an authoritative review). While multipole sources can also be assumed, it is usually the case that the inherent noise associated with empirical measurements mask the

higher terms of the multipole expansion equations, and the first term, that of a dipole, suffices to account for the data. Of course, this solution is subject to verification by other means. These may entail performing similar experiments on humans having known brain damage, e.g., a surgically removed temporal lobe for the treatment of epilepsy, or damage produced by disease and identified by means of CT scans. In such experiments the investigator may examine how the distribution of potentials associated with a particular component differs from the scalp distribution observed in normal subjects. In another approach, for medical reasons electrodes are implanted in the brain, and the patient is presented with a particular experimental task. The variation in potential gradients along the length of a string of recording electrodes is studied in conjunction with scalp potentials, and inferences made about the site or sites at which electrical events that give rise to particular scalp-recorded components (cf McCarthy and Wood, 1985).

At this point it is worth noting that the EEG and ERP methods are becoming much more powerful as a result of the recent conceptual advances. These include the development of reference-free recording techniques, the application of current source density techniques, the use of MRI in constructing more realistic models of the head, and so on. It seems likely that future research in this general area will necessarily involve

the use of very large arrays of electrodes and of more powerful computational techniques. Moreover, the analysis of scalp-recorded electrical data will increasingly depend upon the the use of data obtained via other technologies. Neuromagnetic methods are among these complementary technologies.

Neuromagnetism entails measuring the magnetic fields associated with the flow of ionic currents along the lengths of neurons. This technique is completely passive since it involves detecting magnetic fields that naturally accompany normal neural activity. Also, the precision with which active regions of the brain can be located is competitive with that of PET scan, and the ability to resolve active regions from each other is very fine - being on the order of 3 millimeters. Finally, neuromagnetic fields can be studied as they change from one instant to another - a degree of temporal resolution that is much finer than that afforded by PET scan, which is limited by the long half-life of the radioactive substance in the patient's blood. However, it should be noted that some regions of the brain are undoubtedly magnetically "silent", and PET may well be the only means to study their activity.

It is well known that the cell membranes of neurons may be depolarized or hyperpolarized by various neurotransmitters. When the membrane of a dendrite is so depolarized, there is a radial flow of current across the membrane, and this sets up a

potential differences along its length, which results in the flow of ionic current within and along the dendrite. Since every moving electrical charge is accompanied by a magnetic field, such a field surrounds the dendrite of the active neuron. Neurons of the cerebral cortex tend to be aligned at right angles to the surface of the cortex. When several thousand such neurons are active during the same period of time, the field encircling all of them is simply the sum of the fields from each neuron. Since even several thousand neurons fill a very small space, when the net field is measured some distance away, they can be treated as though they are a single source - an <u>equivalent current dipole</u>. This type of source can be visualized as a very small segment of current. With such a source oriented tangentially with respect to the surface of the skull, its encircling field will emerge from the head at one place and reenter at another place (<u>see Figure 1</u>). Neurons of the cortex in the sulci and fissures of the brain satisfy this requirement of being tangential to the skull.

The field produced by activity of small populations of neurons is about one billionth the strength of the earth's steady field, and many orders of magnitude weaker than the fields associated with machinery and electrical equipment in a normal laboratory or hospital environment. Consequently, detecting these weak neuromagnetic fields requires the use of

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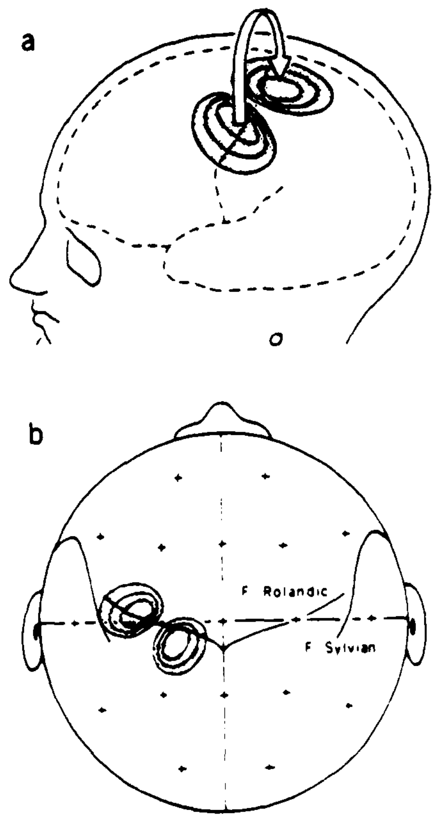


Figure 1

enormously sensitive instruments that discriminate against fields from distant sources. This was accomplished (Brenner, et al., 1975) by using superconducting instruments (composed of devices that have no resistance to electricity when kept at the temperature of liquid helium - about -269 deg C). The heart of these instruments is the SQUID, which is an acronym for "superconducting quantum interference device." The SQUID and other components of the Neuromagnetometer are immersed in liquid helium within a fiberglass dewar (a kind of thermos bottle), similar to that shown in Figure 2. The field associated with neural activity is sensed by the Neuromagnetometer, whose output is proportional to the strength of the field it detects.

The first Neuromagnetometer of this type contained only one SQUID, and was able to measure the field at one place at a time outside the skull. By moving the dewar around, it was possible to map the field at many places outide the head. The main advantage of this stems from the fact that the field normal to the head is competely unaffected by tissues lying between the active neurons and the sensor. Conventional electrical measurements, as in the EEG, are strongly affected by layers of different conductivity within the head, as well as by apertures within the skull, e.g., the orbits of the eyes (Nunez, 1981). For this and other reasons, it is not so easy to compute the location of an active source from the pattern of electrical

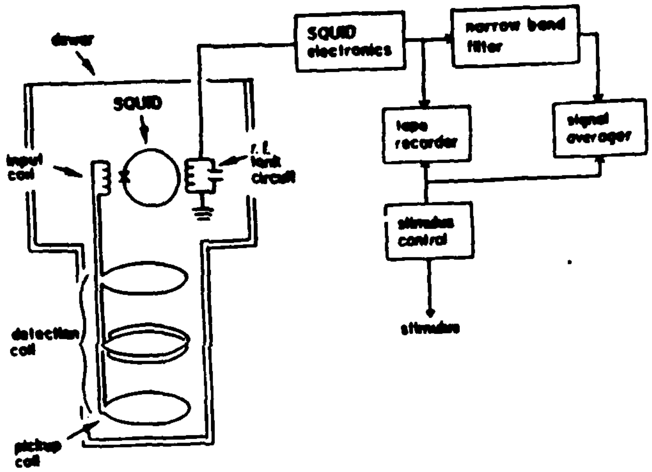


Figure 2. A SQUID system indluding a second order gradiometer as a flux transporter.

potentials on the scalp as it is to make these computations from the field pattern.

Typical field patterns are shown in Figure 3, which depicts "isofield contours." The field strength at any point along one of these contours is the same as it is at any other point. These particular plots are quite similar to the isofield contours that would be produced by a theoretical point current dipole lying a few centimeters under the scalp, just halfway between the line connecting the two field extrema, i.e., where the strength of the field is maximum where it emerges from the head and where it reenters the head. In fact it is quite easy to compute the position of this equivalent current dipole source in three dimensions from the properties of its field pattern. In the instance of Figure 3 we show plots associated with sources activated by acoustic stimuli of different frequencies (Romani, et al., 1982). Since the spread between the field extrema increases with increased frequency of the tonal stimuli, it follows that the depth of the source increases along the floor of the lateral sulcus. If we also take account of the changes in lateral position of the source as the frequency of the stimulus is changed, the cumulative variation of position of the source is shown to increase linearly with the logarithm of the frequency of the tone. This establishes that an equal number of neurons is devoted to each octave of the acoustic range we

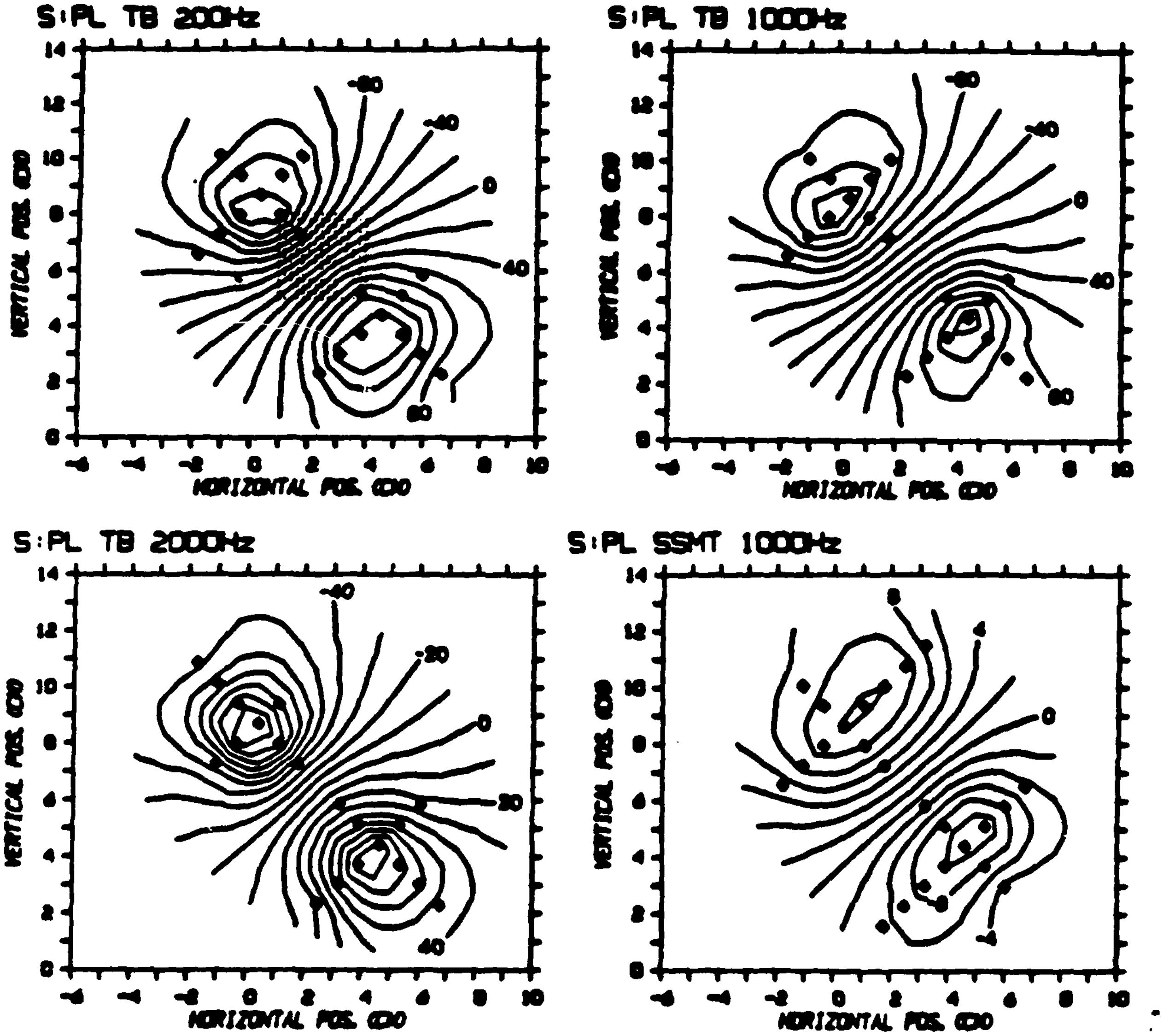


Fig. 3. (TB) Observed field patterns for the 100 ms component of the transient response to a tone burst of 200, 1000 and 2000 Hz respectively; (SSMT) observed field pattern for a steady-state amplitude-modulated tone of 1000 Hz. The origin of the coordinate system is the ear canal, with the horizontal position measured toward the outer canthus of the eye and the vertical position measured perpendicular to this line.

studied. Also, computations based upon assumed cell dimensions and electrical properties indicate that the number of neurons that contribute to each "source" totals about 50,000. It can be seen from this graph that the sources can be resolved from each other (when they are active at different times), even though their physical separation along the cortex is as small as 3 millimeters.

We have obtained similarly dramatic results in studies of the visual system and of the somatosensory system. For example, in the somatosensory system Okada et al. (1983a) resolved regions of the brain that are selectively activated by stimulation of the thumb, index finger, little finger and ankle. Moreover, Okada, et al. (1982) located a region of the brain which became active just prior to the voluntary flexion of a finger, and another region that became active during finger flexion. The latter was presumably due to proprioceptive feedback to the somatosensory cortex, which is posterior to the motor cortex.

Extremely promising results have already been obtained in studies of brain activity related to the performance of cognitive tasks. These include a study of the so-called "P300" component of the ERP, which ocurs about 300 to 400 milliseconds after an infrequently occurring ("odd") event. P300 is of great importance to cognitive psychophysiologists, and our finding

that source of this response appears to lie in or near the hippocampal formation (Okada, et al., 1983b). This establishes that it is possible to detect magnetic activity of at least some subcortical regions of the brain. Also, when a subject is selectively attending to a train of auditory stimuli, while ignoring a similar train presented to the opposite ear, the response of one region of the auditory cortex of one hemisphere is enhanced as compared to the response to the same stimulus train when it is ignored. This particular experiment, which will be described in greater detail in the next section of this report, allowed to to resolve one question as to the source of the N100 component of the ERP. The enhancement of N100 noted by Hillyard and his colleagues during selective attention tasks (cf Hillyard, et al., 1973) is primarily due to the modulation of activity of auditory cortex, and not the the concurrent activation of some more remote source, e.g., in the frontal cortex.

Most of the work described in this Background section was done with a single SQUID sensor. During the past year virtually all of our work was done using a system composed of five sensors. In a short time the NYU Medical Center will be using a 14 channel system in clinical trials and it will be used by our group for research related to the present project. This will be supplanted by a system composed of 100 or more channels in about

three years, allowing us to do a complete neuromagnetic scan at one time.

The scan will provide us with enough data to identify the presence and locations and interactions of sources that are concurrently active at many places in the brain. One of long term goals is to display these sources within an MRI-generated image of the head, perhaps using intensity to represent amount neural activity (current dipole moment) and color to indicate the relative timing of the activity of different sources. Ultimately, images such as these will be rendered in three dimensions and will be rotatable. With these images, and a base of normative data, the investigator will be able to examine the interior workings of the brain, and to relate the observed pattern of activity to the performance of cognitive tasks, workload and perception. It will also make it possible to better interpret data obtained using the ERP and EEG measures made under comparable conditions.

TECHNICAL REPORT

Progress was made on several fronts during the past year. First, we completed an experiment on selective auditory attention using a paradigm that was described in our last proposal. This experiment is described in detail below. Second, we designed and implemented an experiment on selective visual

attention. This experiment is still underway. It too is described in this section. Third, we collaborated with T. Picton and R. Naatanen in designing an experiment that would permit us to make direct comparisons between selective attention and negativity mismatch ERP experiments. The programming for this experiment is underway. Our P300 work has progressed too slowly, and we are now planning a new approach to avoid the pitfalls of trying to implement the McCarthy and Donchin paradigm. The pitfalls and the proposed remedies are described here too.

In addition to the experimental work, we upgraded our laboratory to make other experiments possible. Furthermore, we made progress in developing methods for analyzing neuromagnetic data. This too is described below. We also developed a method for digitizing the human head, and this will make it possible for us to compare and evaluate the effect of realistic head shapes on the accuracy of our source locating algorithms. Finally, and really only incidentally, we were able to make an empirical test of the potential accuracy with which sources can be located within the human body using a neuromagnetometer. This is described later as <u>Project Haystack</u>.

1. <u>Selective Auditory Attention</u>:

The work described here was done in conjuction with Sarah Curtis, a graduate student in the Neuromagnetism Laboratory. It

is the basis for her doctoral dissertation, which is now being written.

1.1 Background:

Several major theories have been proposed to account for the fact that one may attend to a series of events, e.g., a monologue, despite the fact that many other conversations are taking place at the same time. This is the well known cocktail party effect, and it led to extensive experimentation using the dichotic listening paradigm. Some of the names that are associated with this work are Cherry, Moray, Broadbent, and Treisman. Similar work employing the dichotic listening paradigm while measuring ERPs was conducted by Hillyard, Picton, and others.

A number of theoretical issues are associated with the study of selective attention. These are amply treated in many secondary sources, so we shall provide only a brief overview here. The main reason for this is that it illustrates how recording of brain activity may serve a useful purpose in resolving problems of cognitive psychology.

According to one view, selective attention is made possible by a filtering process in which signals coming from a sense organ are attenuated when ignored, or enhanced when being attended to. This may occur very early in the sensory pathway (cf. Hernandez-Peon, et al., 1956) where efferent fibers act on

the sense organ itself. A more sophisticated theory would place the filter at a higher level than that of the sense organ. Sensory data get to the brain, but are not processed in any great detail when something else is going on that is of greater interest (Broadbent, 1957). Nowadays it is believed that the filtering occurs after a good deal of processing has gone on (cf.Tresiman and Geffen, 1967). Thus, unattended speech is not analyzed to the same degree as attended speech, especially if there are strong physical differences between the two messages. However, selection may also take place based upon grammatical content of the speech. This suggests a high level of processing even prior to the perception of the speech itself. This places the filter after the sense organ and peripheral pathways, but prior to perception. By contrast, Deutsch and Deutsch (1963) place the filter between a response and an input already analyzed for meaning. These two views represent what Neisser (1967) refers to as stimulus set and response set. While there are other theoretical issues and points of view that must be considered when dealing with attention, it may well be that recording of brain activity may reveal situations in which these two different kinds of "set" are operating.

Hillyard and his colleagues have already shown that selective attention during a dichotic listening task has no differential effect whatsoever on the auditory brainstem evoked

potential. This would rule out primitive theories such as that proposed by Hernandez-Peon. Effects of selective attention are associated with the N100 component, and seem to begin about 50 msec after stimulation. The negativity difference wave derived by subtracting responses evoked by unattended stimuli from responses evoked by attended stimuli in a dichotic listening task shows a striking effect of selective attention. However, the issue remains, is this difference wave a sign of activity of some novel source (say, in the frontal cortex, as has been suggested by Picton, among others) which comes into play during attention, or is it due to the modulation of activity of the auditory cortex by attention? If the latter hypothesis is confirmed, it would suggest that the filter is placed at an early stage, prior to a complete analysis for meaning. If other sources are implicated, then a response set theory might still be viable for the dichotic listening situation. (At this point a caveat is in order. That is, if one of the hypotheses is confirmed it does not prove that the other hypothesis is innapplicable to other situations. In fact, attention is a complicated process and could well entail "software" assignments of filter location, depending upon the nature of the task).

1.2 Dichotic Listening Experiment:

Method: Three subjects listened to tone pips presented to the two ears via an airline headset. The pips presented to one

ear had a repetition rate of 3 pips per second, while those presented to the other had a repetition rate of 3.5 pips per second. Since these two repetition rates were not harmonics of each other, it was possible to recover responses at 3 Hz and its higher harmonics separately from those at 3.5 Hz and its higher harmonics simply by averaging with two different sweep (epoch) durations.

The tone pips presented to one ear had two different carrier frequencies. These were 1000 Hz and 1050 Hz. These two frequencies were presented in a pseudorandom sequence, i.e., the order of the tone burst frequencies was randomized, but after a number of them had been presented, the random sequence was repeated. A similar procedure was used with the tone pips presented to the other ear. The main difference was that the carrier frequencies were at 3000 Hz and at 3050 Hz, These too were presented in a pseudorandom sequence, albeit independent of the sequence presented to the other ear.

Since the repetition of the sequence of tone bursts was not signalled to the subject in any way (the repetition was "seamless"), at first there appeared to be no particular recognizeable pattern. The subject's task was to detect the length of one of the two sequences before it was repeated again. The sequence presented to the other ear was to be ignored. Naturally, on half the trials the subject attended to the tones

of higher pitch, and, on the other half of the trials, to the tones of lower pitch.

This turned out to be a particularly demanding task since the subject had to virtually "shadow" the attended sequence. Retrospective reports indicate that all of the subjects developed the same basic strategy for performing the task. That is, they learned to listen to a unique chunk of pips of the same pitch, e.g., 3 or 4. Then they started counting pips until the heard this sequence again. They then monitored the sequence to be sure that it had the same pattern between the distinctive chunks before making their decision. This strategy made it possible for subjects who were previously unable to do the task when more than 10 or 15 pips comprised a sequence, to perform the task with 40 - 50 pips per sequence. (As we shall see later on, we now have a procedure which makes it impossible for subjects to ignore any tone bursts between critical chunks, as may be possible in the present task. Moreover, this procedure makes it possible for us to do more than make the binary decision as to whether the subject was right or wrong in his or her count).

While the subject was attending to the signals presented to one ear, our five-channel neuromagnetometer was placed at one of several different positions over one side of the head. (For more details on the neuromagnetometer see Section 3.2 on P300 in this

report). Since it required a total of about 900-1000 tone bursts before subjects gave accurate answers (within 1 of the actual count), the outputs of all five channels was averaged for about five minutes over several repeated trials of about 500 tone bursts each. Hence there were 2000 to 4000 replications of each tone bursts in each grand average. Measurements were made over the left and right hemispheres, with the attended stimulus on either the ipsilateral or contralateral side. Responses to both the attended and unattended stimulus were recorded from both sides of the head, from approximately 60 positions on each side. This sufficed for us to compute isofield contour maps for each significant component in the response, and to determine if the responses in the vicinity of the field extrema differed in amplitude or latency, depending upon the state of attention. We were also able to determine if the effect of attention in this task was lateralized in any way.

Results: Typical waveforms associated with responses to the 3 pip per sec stimuli and the 3.5 pip per sec stimuli are shown in Figures 4, 5, and 6, where responses from each of the five channels to ignored and attended stimuli are recorded from the same places, although at different times. Two peaks can be observed in these tracings, and we shall tentatively identify them as 'N1' and 'P2' (see Section 1.3 for justification of this labelling of the peaks). An analysis of variance was performed

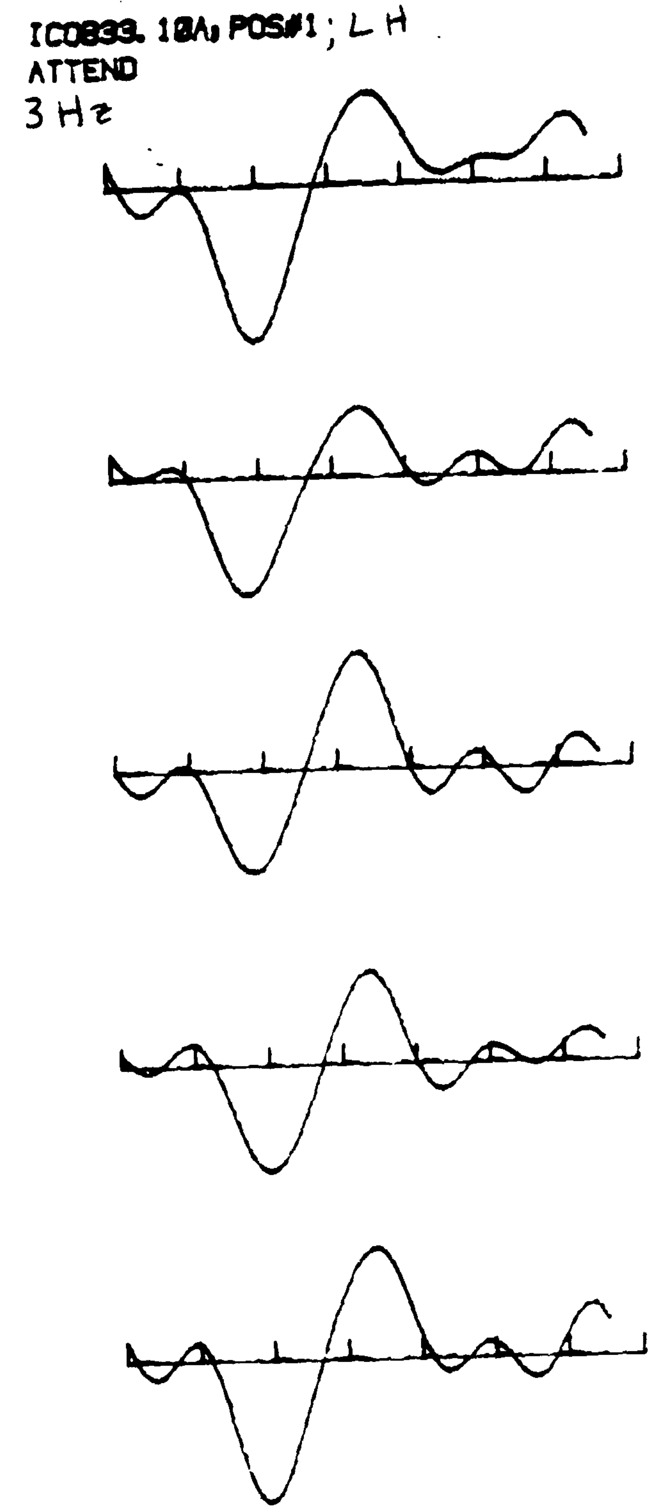


Figure 4

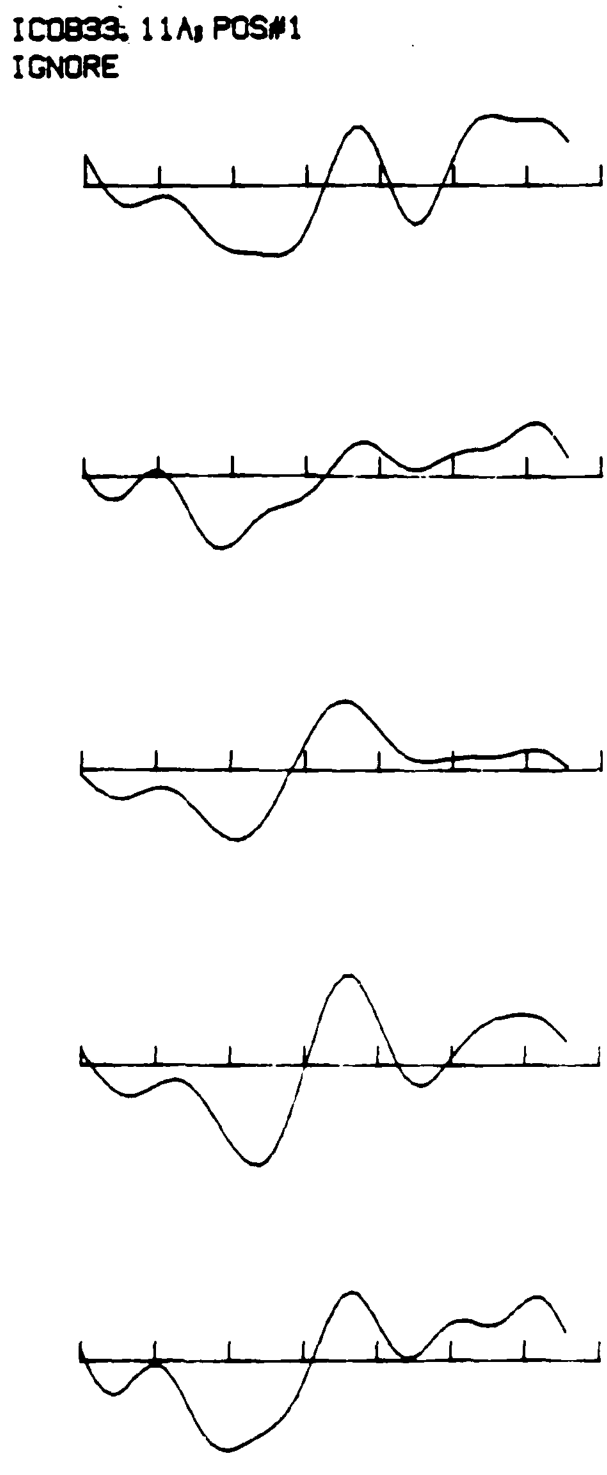


Figure 5

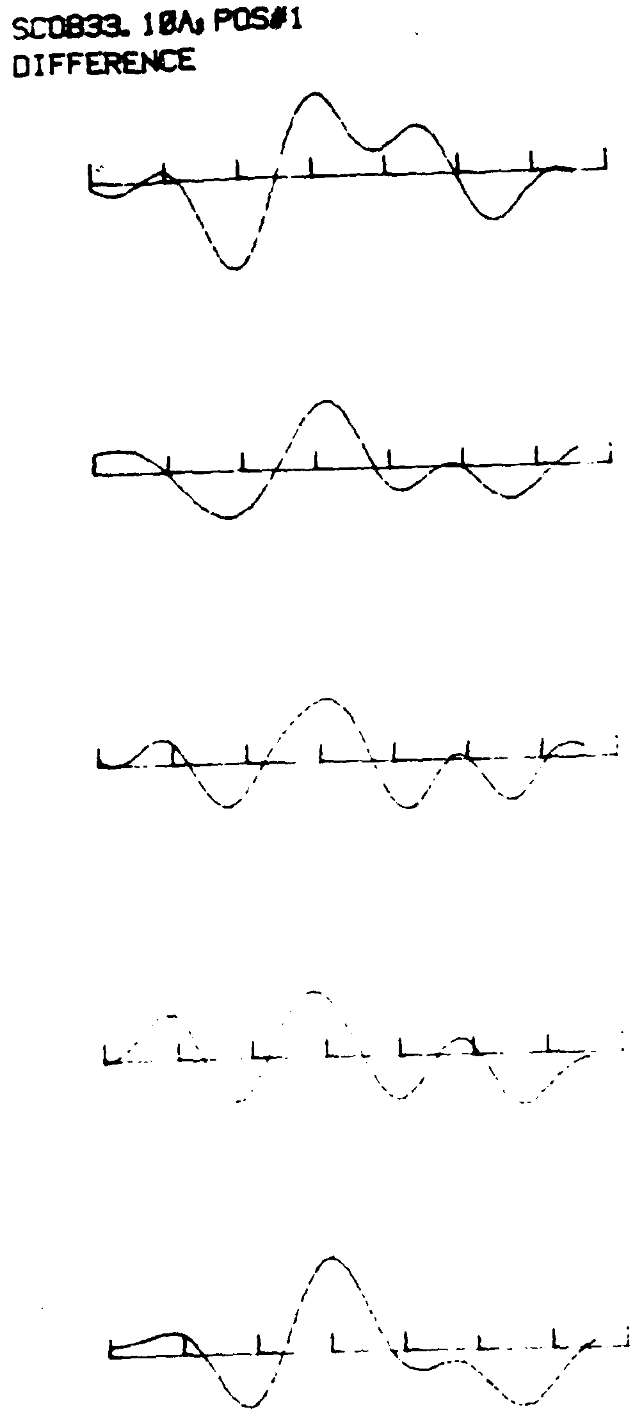


Figure 6

after editing out all data that did not exceed the level of the backgroud noise. The rationale behind this is that where no responses can be recorded, the sensors are presumably not close enough to the source to pick up its field. Hence, by including such data we would simply be comparing noise with noise. Even so, this left many data points for the analysis. These points were the peak amplitudes of the two salient components of the responses under conditions of attending and ignoring. The latter conditions are referred to hereafter as reflecting <u>instructions</u>. In addition to instructions, other sources of variance were <u>subjects</u>, <u>hemisphere</u>, <u>stimulus</u> (3 pips/sec vs 3.5 pips/sec), <u>channel</u> (the 5 detector channels were always in somewhat different positions), and <u>location</u> (data recorded near one extremum were compared with those recorded near the opposed extremum). Subjects were the random variable.

Unsurprisingly, the subjects differed significantly from each other. Also, the effect of instructions was significant, with p=.0278. Also unsurprisingly, the channels differed from each other with p=.0138. None of the other main effects were significant, and this included that of hemisphere. Of course, a larger subject population may have revealed some interaction between hemisphere and the effect of instruction to attend. None of the lower-order interactions reached significance. While some of the higher-order interactions were significant, these are

probably uninterpretable. A full account of this analysis will soon be published.

As shown in Figures 7 and 8, we plotted isofield contours for both peaks in these responses. The figures are samples, but the same applies to all of the data, namely, we were unable to resolve the differences in locations of 'N1' and 'P2'. Previously (Pellizone, et al., 1985) reported a very careful set of measurements on the classic N1 and P2 on one subject and found that their sources were nearly 1 cm apart near the lateral sulcus. Apparently, positioning errors in this experiment made this distinction impossible. Similarly, were were unable to resolve separated sources for 'N1' (or 'P2') when subjects attended to the stimulus and ignored it. Therefore, we cannot reject the hypothesis that the source of our components during attention is the same as the source when the stimulus is being ignored. There is no sign of any other tangential source when the attention effect is present.

The main point to be drawn from this is that both 'N1' and 'P2' are affected by attention, and subjects differ in the magnitudes of their responses. However, as the reader is undoubtedly aware, the responses obtained in this experiment may be aptly described as being quasi steady state. The classic N1 and P2 are found in transient evoked responses, and the peaks in the responses recorded here may therefore be only coincidentally

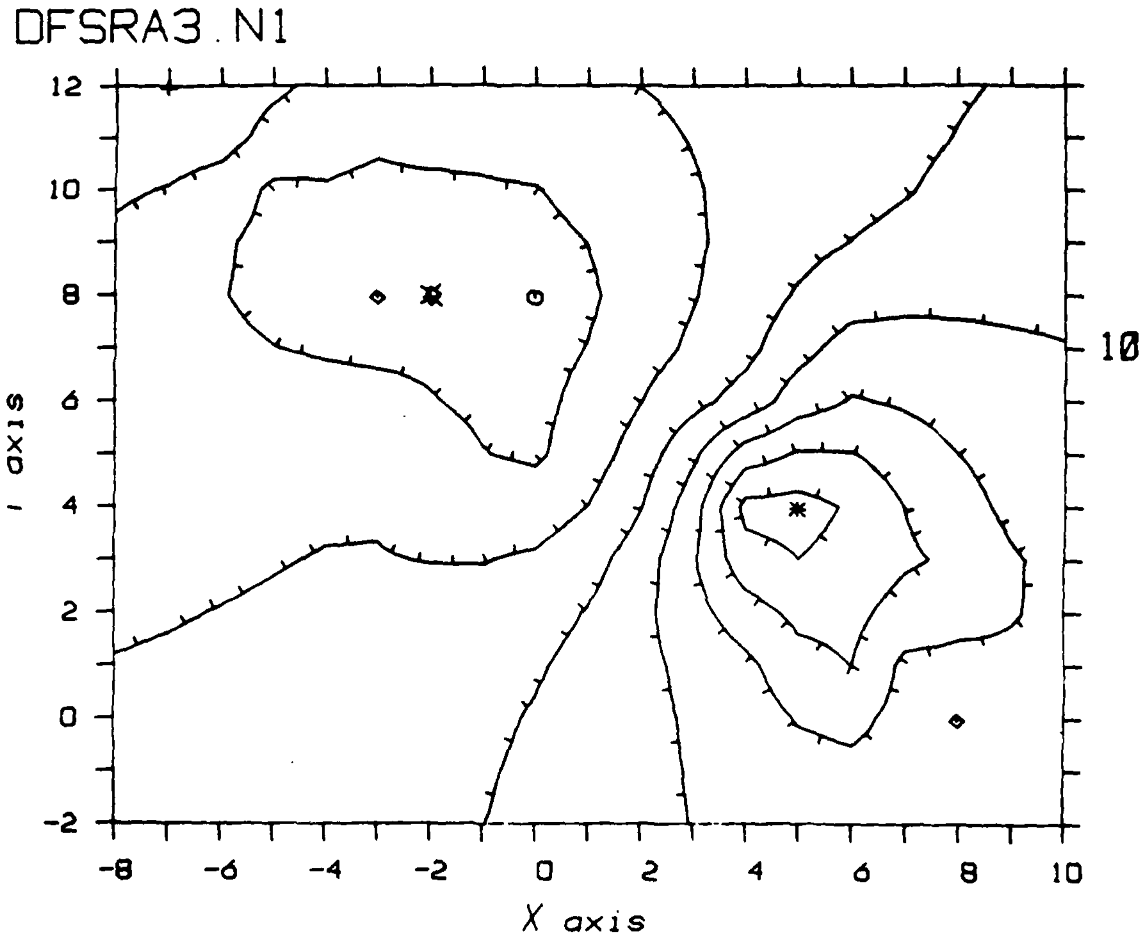


Figure 7

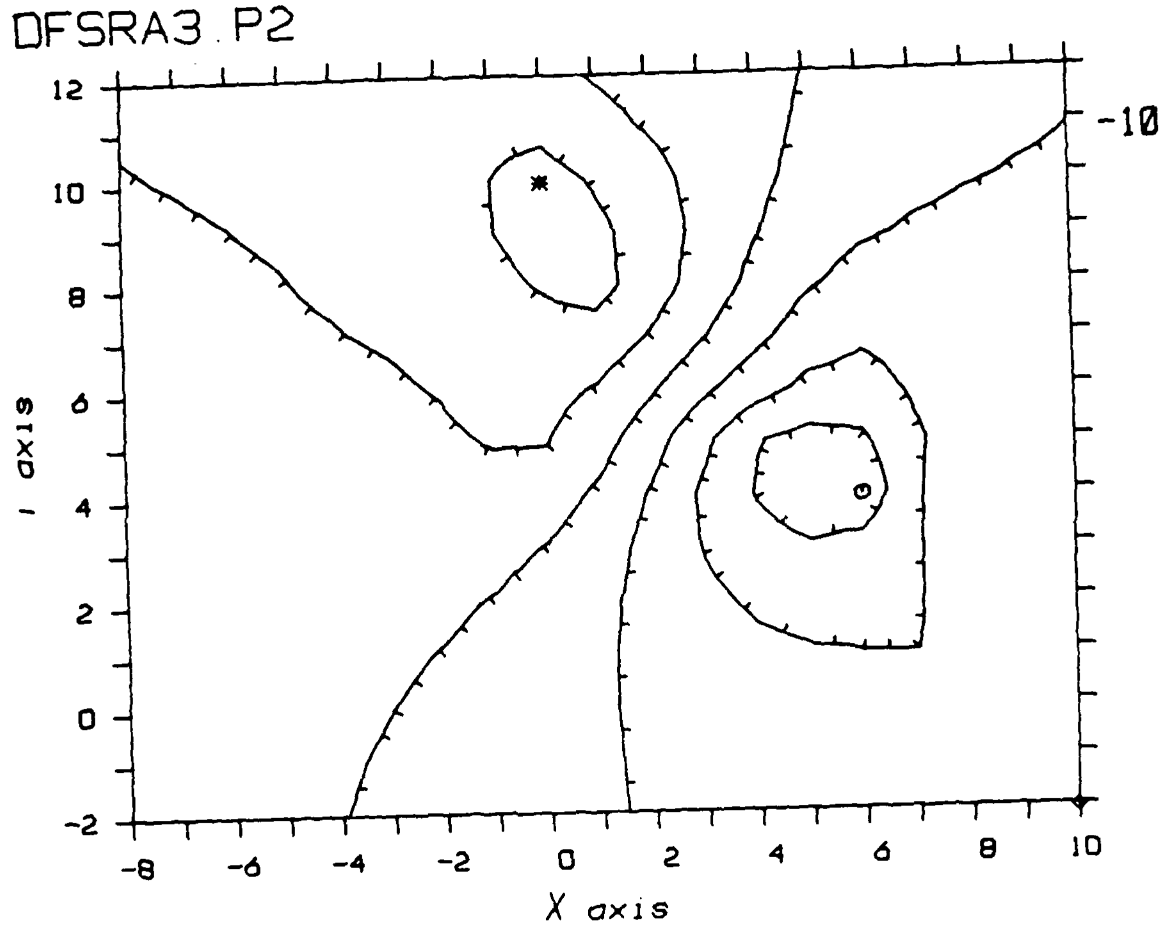


Figure 8

related to the classic components. The next experiment was designed to determine if 'N1' and 'P2' of the quasi steady state responses have the same source as the N1 and P2 obtained in transient evoked response experiments.

1.3 Transient Response Control:

Method: In this experiment two of the subjects used in the first experiment were employed once again. They were asked to lie comfortably on a table while neuromagnetic responses were recorded from many different positions on one side of the head. The responses were evoked by 1500 Hz tone bursts, similar to those of the preceding experiment. The ISI was 1 sec +/- 500 msec and each response was the average of 200 responses. This revealed the classic evoked field pattern, which had already been described by many investigators. As shown in Figure 9 the response contains easily identified N1 and P2 components. The many measurements made about the side of the head made it possible for us to fit isofield contours corresponding the time of the peaks of these two components. A sample plot of N1 is shown in Figure 10. Using the data of the preceding experiment we plotted the isofield contour maps for 'N1' and 'P2' of responses obtained on the same side of the head while the subject was attending to the stimulus. These were already shown as Figure 7 and 8. The sources of 'N1' and N1, as well as 'P2' and P2 cannot be resolved from each other in these sets of

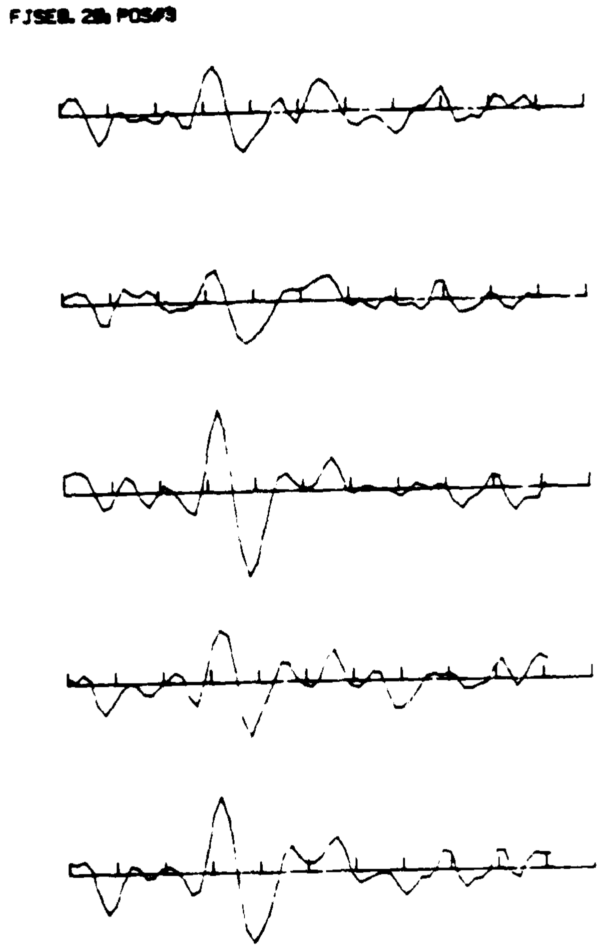


Figure 9

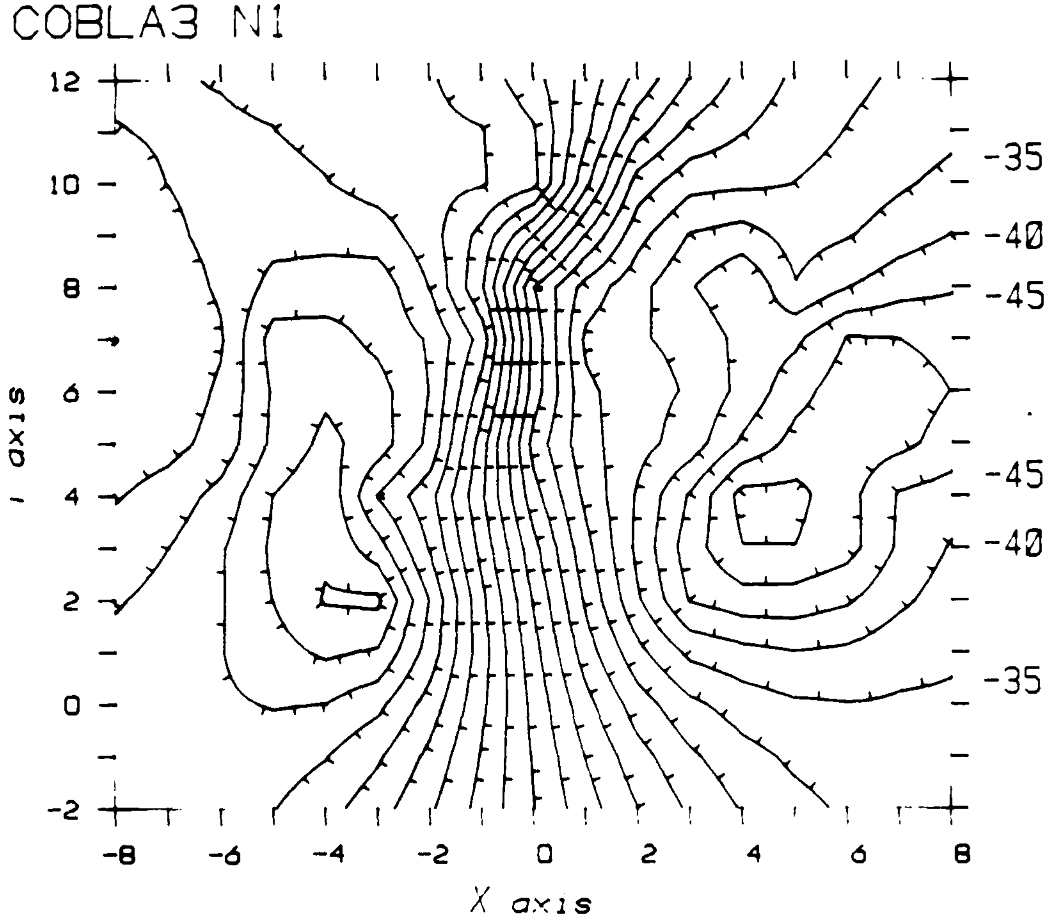


Figure 10

plots. The positioning errors involved in this particular experiment make it impossible to tell if one source is involved or if there are two sources separated by a distance not greater than 1 cm. Therefore, we cannot reject the hypothesis that the source of N1 is also the source of 'N1'.

Taken together with the preceding experiment, it must be concluded that N1 is generated by a source in or near the auditory cortex and its activity is modulated by attention. There is no sign of the activation of some other tangential source during attention. Widespread scanning of the head failed to reveal any such effect. Of course, we cannot rule out the existence of some independent radial source which does not produce a detectable external field.

1.4 Loudness Control Experiment:

One question of concern has to do with the effect of the physical properties of the stimulus on attention related evoked fields. This small experiment represents a preliminary effort to explore this facet of the problem, which is important because it is widely believed that N1 is some combination of endogenous and exogenous phenomena.

Method: Once again, two subjects were employed. The experiment was essentially the same as that described under Section 1.2, except for one minor change. In this case the

stimuli presented to the two ears were matched in subjective loudness by the subjects. The experiment was repeated using both carefully matched stimuli, and then repeated again with one or the other of the two stimuli attenuated in intensity by 20 dB. Thus, there were 3 basic conditions. In one the loudness was matched in both ears. In another the loudness of one stimulus was attenuated for one ear and not the other. In the third the loud stimulus was attenuated by 20 dB, and the previously attenuated stimulus was made as loud as it was originally.

Results: As before, the two subjects differed significantly from each other in the magnitudes of their responses. Also, there was a significant effect of instruction ($p=0.004$). The difference in loudness of the physical stimuli made no difference whatsoever. Consequently, despite a very discernible change in the physical properties of the stimulus, there was no systematic change in the effect of selective attention.

1.5 Message vs. Ear

Effects similar to those obtained in dichotic listening experiments can also be obtained when both messages are presented to one ear. To compensate for the fact that the subject can no longer "tag" a particular message by the ear to which it is presented, it is of some value to make the messages very distinctive, e.g., have a female voice recite one of the messages while a male voice recites the other message.

In an extensive series of preliminary experiments we had already presented both of our "messages" to both ears, although one of the messages was louder in one ear, while the other was louder in the other ear. This was done by using two loudspeakers, with one closer to one ear and the other closer to the other. This gave us essentially the same results as those described in Section 1.2. We decided to repeat this procedure, but with the two loudspeakers mounted side-by-side and the tones matched for subjective loudness. The purpose was to see if identification of a message with a channel (ear) facilitates the attention effect.

Method: As before, two subjects were employed. Also, the prcedures were the same as above, the only difference being that the sequences of tones were presented by piezoelectric speakers mounted side-by-side near the subject's head. A block of trials was also conducted in which the stimuli were presented in the normal dichotic manner.

Results: There was no difference between the effect of dichotic listening and monaural listening to the two trains of stimuli. As we prepare this report, it is evident that there is an error in the analysis of variance. Computers simply cannot be trusted. The data show clearly that the effect of attention is equally good for both monaural and dichotic listening, but the table of the analysis shows no significant differences. We

haven't the time to clarify this issue now, but will do so in a supplementary report.

1.6 Plans for a New Collaborative Experiment:

Terry Picton and Risto Naatanen were visiting scholars at the Neurosciences Institute at Rockefeller University during the last month of this reporting period. We had contacts with Picton in Bogota, Colombia last year, and spent a good deal of time with Naatanen in Helsinki in August and September of 1985. (In fact, one of us was a member of the dissertation committee of one of Naatanan's students and also attended a small conference at Rockefeller with Picton, Naatanen, Hillyard, Vaughan, Wood, and McCarthy). This led us to meet on several occassions while they were both in New York. It became apparent that we had many common interests, ranging from the original work of Hillyard and Picton to the mismatch negativity discovery of Naatanen. In our meetings we decided that it would be possible to conduct an experiment using conventional methods (by "conventionl methods" we mean the experimental procedures used in the not too distant past by Hillyard and by Naatanen to study the negativitiy difference and the mismatch negativity phenomena, as opposed to the methods we used in the experiments described above). While none of us expect that the N1 and 'N1' identity postulated above is necessarily incorrect, we all agreed that a common methodology would put the issue to rest. Coupled with a more

precise positioning procedure, which we have already developed, commonality or differences in source location should be discernible. The experiment we settled upon can be implelemented easily, since Picton already has a Fortran program that can be used to generate stimuli. We need to complement the program with an analysis procedure capable of accepting input from 5 channels at once. This requires minor changes. However, our computer lacks the memory capacity to handle both the program and the data acquisition and analysis. To accomplish this we needed a Winchester hard disc, and, as a result, we received permission from AFOSR to reallocate funds for capital equipment to this purpose. We received permission to so use the funds only recently. Some of the needed equipment is on-hand and the rest will be delivered shortly. Meanwhile, Dr. Aries Arditi of the New York Association for the Blind and an associate at NYU has agreed to adapt Picton's program to our computer system. This will be at no cost to the Air Force. As soon as this is completed, we will be in touch with Drs. Picton and Naatanen and will conduct the proposed experiment. The results will be described in our next report. It is our conjecture that both the mismatch negativity and the negativity difference wave have somewhat different sources in the auditory cortex.

2.0 Selective Visual Attention

During the past year we made progress in developing procedures for studying selective visual attention. Preliminary results strongly suggest that the visual system is affected by selective attention in a manner that is comparable to what has already been found in the auditory system. At the present time we feel that each of the primary sensory receiving areas is capable of filtering incoming information for purposes of selective attention. These functions may not occur precisely where the afferent volley first arrives at the receiving area, but it may occur only a few synapses later. Thus, the N1 found in auditory experiments has its source near the tonotopically organized portion of the auditory cortex, and it is extremely labile in terms of the effects of attention. Preliminary evidence suggests that a similar state of affairs exists in the visual system.

Apart from the foregoing conjectural statement, our work in selective visual attention has led to new experimental methods that can be applied to the auditory system as well. The major conceptual contribution to this effort came from Risto Ilmoniemi of Helsinki, who is doing postdoctoral studies in our laboratory. The research is being conducted by Bruce Luber, who is also responsible for programming the computer. Mr. Luber is a graduate student working in our laboratory.

Ilmoniemi's suggestion was simply that we present a random series of stimuli and, after some interval of time, the series is terminated and the subject asked to tell the experimenter what the last four items in the series were. Elaborating on this idea, we present a grating of a particular spatial frequency (e.g., 1.5 c/d) for a brief period of time and then, after a blank interval, present another grating which may be the same as the first or it may be 3.0 c/d. These two are presented at random for a randomly selected period of from 4 to 40 sec. with a repetition rate of 3 Hz. At the same time, another grating is presented in a similar manner but it is either 4 c/d or 8 c/d and its repetition rate is 2.5 Hz. The two gratings are presented one above the other, with fixation between them and about 0.5 deg to one side. This results in visual signals from the gratings going adjacent regions in one hemisphere. The subject attends to one of the two patterns and attempts to keep track of the series in the pattern so that he or she can report correctly on the sequence of the last four or five gratings (e.g., "two thick bar patterns followed by one thin bar, and then another thick bar pattern.") The program is so designed that the correct answer is stored, and the response is also stored. Therefore, we can compare correct and incorrect responses. Thus far we have found a substantial enhancement in the evoked field from the hemisphere receiving the signals.

However, we have not yet gone beyond the occipital region, and we do need to conduct many more measurements. The main advantage of this procedure is that it seems to insure continuous attention to one of the gratings and it limits the strategies that subjects can employ. Also, we can study effects within and across hemispheres. Finally, we can consider accuracy as reflecting different degrees of performance, and compare responses with these degrees of performance.

3. P300 Studies

3.1 Background:

This section describes an ongoing effort in considerable detail. It should be considered to be a preliminary report which covers a joint effort by the University of Illinois and NYU that was sponsored by AFOSR. It represents the first full-scale use of our five-channel system (see below), and the first extensive coordinated recording of multiple EEG channels at the same time. This turned out to be a much more complicated process than we had anticipated, and the total configuration of systems had many flaws. These had to be worked throughly before an experiment could be conducted, and this resulted in a serious shortfall in time available for experimentation. Hence, the results are not as impressive as we had hoped they would be. In view of the inconclusive nature of the collaboration, we are obligated to

continue the project along lines that will lead to the results we sought at the outset. However, this continued effort, which will be described below, will be conducted exclusively by our own group. Dr. Donchin of the University of Illinois will be consulted before a final report is submitted.

Okada, Kaufman and Williamson (1982) described a magnetic counterpart to the electrical P300, which was measured while the subject was counting infrequently presented visual stimuli. These stimuli were gratings having a spatial frequency other than that of a frequently presented grating, as in a typical "odd ball" experiment. The neuromagnetic field associated with the P300 complex emerged from one side of the head and reentered the head in the occipital region. At the same time, the contralateral field emerged from the occipital region and reentered in the temporal region on the other side of the head. The depths and lateral positions of equivalent current dipole sources of these fields were computed using a method described by Williamson and Kaufman (1981). It was concluded that the observed field patterns could be accounted for by two equivalent current dipoles, with one in each hemisphere and located in or near the hippocampal formation.

This result is consistent with recent data obtained by McCarthy and Wood (1985) in epileptics who had electrodes inserted in their brains for diagnostic purposes. However, these

authors point out that their data are consistent not only with the presence of a source in or near the hippocampus, but also with a source in the frontal regions. This conclusion is tentative because of the limited amount of information obtainable from two electrode tracks, and where the precise depths of the active electrodes are not known.

At this point it should be emphasized that the concept of the equivalent current dipole is a convenient heuristic which allows us to account for observed patterns of neuromagnetic fields. The equivalent current dipole is considered to be the "source" of the measured field if the field could be produced by a current dipole in a particular position within the head. It is recognized by all workers in the area that a field which could be produced by a single equivalent current dipole may actually be produced by a number of active sources within the head. This follows from the fact that there is no unique solution to the inverse problem. Even so, if a very large amount of the variance in the P300 phenomenon can be accounted for by postulating an equivalent current dipole source, then it will be possible to test the hypothesis that the phenomenon is due to a unitary underlying process, which remains invariant under conditions that may affect the amplitude, latency or waveform of the observed P300.

To help the reader understand the issues involved, it may be worthwhile to examine the analogy of the "point source" in optics. There is no such thing as a point (dimensionless) source of light in nature. However, some distance from a physically extended source, the distribution of light that it produces may be indistinguishable from the calculated distribution that would be produced by a hypothetical point source. In practice, if the length of a linear extended source is less than one tenth of the distance at which the light it emits is measured, it is safe to assume that the measured distribution of light is emitted by a point source. Similarly, nobody disagrees that a population of a few thousand closely spaced and concurrently active neurons whose electric or magnetic field is measured at a distance that is large relative to the space occupied by the population, is essentially indistinguishable from a point current dipole. The question we are addressing concerns whether or not the magnetic P300 can be viewed as resulting from the activity of such a unitary population of neurons or of a set of closely spaced populations, or if it is necessary to postulate the existence of more than one such population located at relatively widely spaced locations in the brain.

It may well be that P300 is the sum of effects produced by several widely spaced current dipole sources, depending upon the nature of the task being performed. For example, Halgren, et

al. (1980) found steep potential gradients in the vicinity of the hippocampal formation and in amygdala in patients performing an odd ball task. These measurements were possible because these patients also had electrodes implanted in their brains for medical reasons. However, these results implicate the limbic system and not a single nucleus or region of the brain. Also, the time course of the variation in voltage did not correspond precisely with that of the scalp-detected P300. The more recent work of McCarthy and Wood (1985) suggests that there may be at least two sources, one in the vicinity of the hippocampus and the other someplace in the frontal lobes. However, owing to constraints imposed by the need to consider the welfare of the patient, these investigators were unable to do more than examine the potential gradients along only two paths within the brain, and these paths varied across patients and there was some uncertainty about the precise locations of the electrodes within the brain. Also, here too there were differences in the time courses of the P300 detected at or near the surface and similar phenomena detected at greater depth. Thus, we cannot rule out the possibility that the scalp-detected P300 is not a sign of activity of a single mechanism, and multiple sources that might contribute to it may vary, depending upon the conditions of the experiment.

It is noteworthy that several different experimental conditions have strong effects on both the latency and amplitude of P300. This raises the possibility that 'P300' in one set of circumstances may have one set of sources, while 'P300' obtained in other experiments may have partly different sources. A good example of this is the experiment by McCarthy and Donchin (1980). Their subjects had to respond to key words in a matrix of letters of the alphabet. Sometimes the matrix contained the word RIGHT and at other times it contained the word LEFT. One of these two words was displayed less frequently than the other, and it thus served the same role as the "odd ball" stimulus in experiments employing simpler stimuli. Three different experimental conditions were employed. In one of these, all of the letters of the matrix were Xs, except for the RIGHT and the LEFT stimuli. This made it easy to see the target words. The subject had to respond to the word RIGHT with his right hand in one series of trials, and with his left hand ("response incompatibility") in another series of trials. This had the effect of increasing reaction time, but it had no effect on P300, which was affected only when the perceptual processing aspect of the task was varied. This was accomplished by embedding the target words in a matrix of various letters which increased the difficulty of perceiving the target words RIGHT and LEFT. The resulting increase in the difficulty of detecting

the target words was also accompanied by an increase in reaction time, but it was also accompanied by a dramatic increase in latency of P300, as well as a reduction in its peak amplitude. This change in P300 was not encountered in the "response incompatiblity" condition, although both response incompatibility and difficulty of detection result in an increase in reaction time. This result leads to the main question addressed by our experiment, namely, are the neural generators of P300 in the non-noise condition (when the target words were embedded in a matrix of Xs) the same as that in the noise condition (where the target words were embedded in random letters, thus making them more difficult to detect)? To answer this question we planned to use the magnetic method conjointly with conventional electrical measurements. These two sets of measurements allow us to determine how well the electrical P300 is correlated with the magnetic, and also to determine if the location of the equivalent current dipole source of the P300 of the EMF is the same under these two conditions.

Before we could proceed with this approach it was first necessary to demonstrate a magnetic P300 effect using stimuli similar to those employed by McCarthy and Donchin. To test our conjecture that the source of the P300 may change with experimental conditions, it is necessary that the basic effect be strong enough so that noise does not mask significant

differences in source location. Thus, our first task is to demonstrate that current dipole sources of the magnetic P300 can be localized reliably when it is affected by the experimental manipulations introduced by McCarthy and Donchin (1980). This is the basis for the pilot experiment described below.

3.1 Visual Odd-Ball Experiment:

Method: The goal of this preliminary experiment was to determine if the stimuli used by McCarthy and Donchin can be used to obtain Event Related Fields (ERFs) comparable to Event Related Potentials (ERPs), including the deflections in the ERP waveform conventionally referred to as "P300." To conduct this experiment we transported the PEARL system and its associated visual display from the University of Illinois to New York University. The PEARL system includes an LSI 11/23 computer, EEG amplifiers and software suitable to averaging responses to stimuli, as well as automatic sensing and editing (eliminating) responses contaminated by eye movement artifacts. The latter were monitored by means of electrodes attached to the skin near the outer canthi of the two eyes. The software also provided the capability for displaying matrices of letters, in this case the latters in the background were all Xs, and the target words were RIGHT and LEFT. As in the original experiment by McCarthy and Donchin, the word LEFT was presented only 20% of the time while the matrices contained the word RIGHT on 80% of the trials. The

task of the subject was to keep count of the randomly occurring odd event (the number of LEFTs). ERPs were recorded between each of three "active" electrodes (at Cz, Fz and Pz) and a cephalic reference electrode.

Concurrently with the recording of the ERPs, the magnetic field normal to the scalp was measured at five different positions at once. This led to the computation of five different average ERFs at the same time as we recorded the average ERPs associated with the odd events and, for comparison purposes, the frequent events. The field measurements had to be replicated many times so that we could generate field maps that allow us to compute the location of the source of the P300 (see below). These measurements were made with a five-sensor neuromagnetometer ("Freddy") described by Pelizzone, et al. (1985). The sensing coils of Freddy were superconducting second order gradiometers with a baseline of 4.0 cm and a coil diameter of 1.5 cm. The gradiometers, associated SQUIDs, and other superconducting electronics were immersed in a bath of liquid helium contained within a fiberglass cryogenic dewar. The gradiometer pick-up coils were located at the four corners of a square, with the 5th coil in the center of the square. The distance between the centers of adjacent pickup coils was 2 cm, and the gradiometers were canted outward by 10 deg relative to the central gradiometer. Since all five sensing elements were

contained within a single cyrogenic dewar, the pickup coils were effectively tangential to the surface of a sphere with a radius of curvature of 10 cm. (The outer surface of the tail section of the dewar had a radius of curvature of 9 cm, and the bottom of the tail section was 1 cm thick). The entire dewar could be moved in its gimballed holder (SCANNER) so that the bottom of its tail section could be moved along a spherical surface having a 9 cm radius of curvature. With the head centered on a 9 cm radius spherical volume, it is possible to move the dewar so that the pick-up coils measure the field at many different positions on the sphere that best fits the head. This permits the use of a sphere model in computing the locations of equivalent current dipole sources associated with the measured fields (Williamson and Kaufman, 1981). In the present experiment the field was measured at 45 positions over the right temporal region, 80 positions over the occipital region, and 90 positions over the left temporal region. Since most of these positions were non-overlapping, the field was measured at approximately 215 distinct locations for subject SG. (A parenthetical note is in order at this point. That is, prior to this experiment we had recognized the value of making repeated measurements by at least one of the five pick-up coils at the same position, thereby enabling us to test the assumption that the response is stationary from one trial to the next. Unfortunately, owing to an oversight, this

was not done. However, in view of the pilot-nature of this experiment, the failure to do this is of little immediate consequence. In more formal experiments, however, this will have to be done.) In any event, the coordinate system used for placing the sensor was referred to the ear canal or to the inion. When measuring the field in the temporal region the horizontal axis was the line joining the ear canal to the outer canthus of the eye. When measuring the field over the occipital region the horiontal axis passed through the inion and was parallel to the horizontal axis for the temporal region, with the midline as the vertical axis. The ear canals were 12.5 cm anterior and 2.5 cm below the inion in subject SG.

In addition to the five gradiometers and associated dcSQUIDs used to detect the fields of interest, the ambient magnetic noise was detected by each of four different "noise" channels. These were composed of rfSQUID magnetometers that measured the ambient field in the X, Y, and Z directions, and a first order gradiometer that measured the field gradient or first spatial derivative of the field along the Z axis. The outputs of these noise channels were given different weights and then subtracted from each of the signal channels. The weightings given these outputs before subtraction from each channels were chosen so that the channels outputs of the channels would be at a minimum when they were in the presence of a uniform field and

when the field had a uniform gradient. The fields for balancing the channels so that they would be insensitive to them were generated by large square (10 ft. per side) Helmholtz coils. The outputs of the signal and noise channels were bandpass filtered between 0.3 and 45 Hz before signal averaging. For the purpose of this experiment, the outputs of the EEG amplifiers were similarly filtered prior to averaging. Responses contaminated by eye movements were eliminated from the EEG recordings. Even though the magnetic responses were not similarly contaminated, those that occurred during detected eye movements were eliminated also. In addition, whenever noise levels exceeded a value that resulted in signal saturation, the epoch in which the event occurred was eliminated too.

In these first studies using the Freddy system we encountered some difficulties associated with using the Rockland filters. These filters have sharp cutoffs and this distorts the waveform of the response so that the 'P300' deflection is shifted. However, by recording a conventionally filtered electrical response (where P300 is recognizeable in accord with conventional criteria) and comparing it to the same recording when it is filtered by the Rocklands during averaging, it was possible to identify the P300 complex in the filtered response with total confidence, despite the distortions introduced by the filters.

More concretely, the potentials were filtered in two different ways before averaging. In one the electrical activity was filtered in the customary manner with a low frequency cutoff of 0.1 Hz and a high frequency cutoff of 50 Hz, with rolloffs of 12 dB per octave. This resulted in minimum distortion of the average waveform. In parallel, the same activity was averaged after being applied to the Rockland filters (bandwidth of 0.3 - 45 Hz and rolloffs of 48 dB per octave). After such filtering, two different waveforms resulted, even though they represented the same electrical response. Although there are substantial differences in these waveforms, one can identify the P300 complex in both waveforms. Therefore, despite the distortion introduced by the Rocklands, we are able to describe the effects of various experimental manipulations on P300.

Results: Given the foregoing description, the results are rather straightforward. As shown in Figure 11, it is clear that magnetic P300 responses to oddball stimuli were much enhanced, as compared with responses to the frequent stimuli. Also, the tracings depicted in Figure 11 were obtained when the five pickup coils were located over the occipital region just to the right of the midline, and over the right temporal region. Similar results were obtained with the pickup coils over the left temporal region (though of opposite polarity to those from over the right temporal region) and over the region slightly to

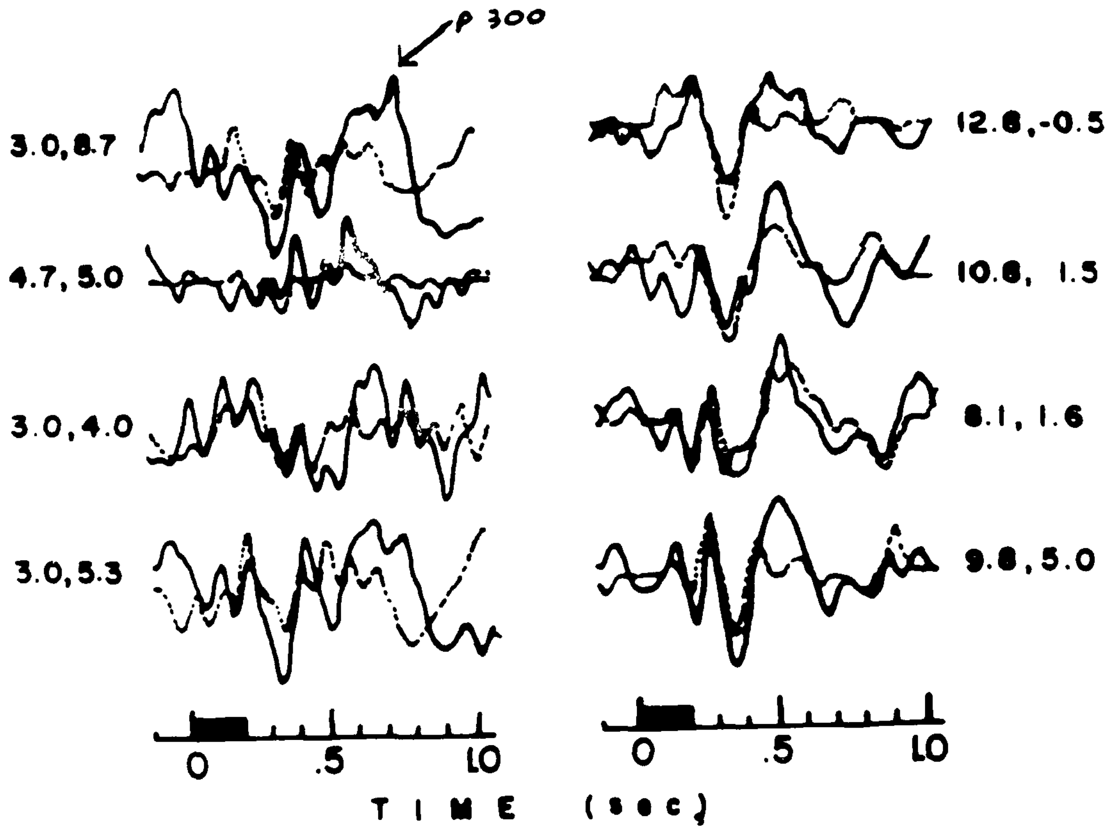
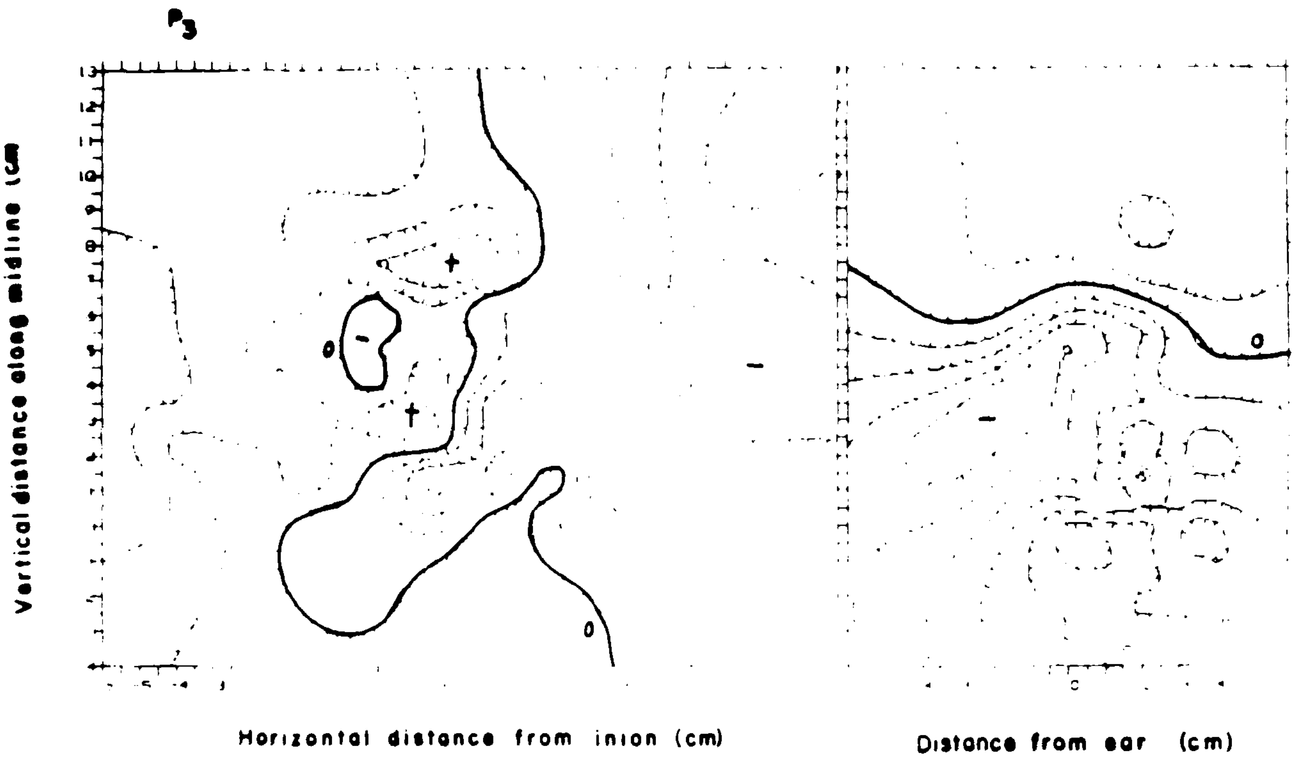

P 300
3.0, 8.7
4.7, 5.0
3.0, 4.0
3.0, 5.3
12.8, -0.5
10.8, 1.5
8.1, 1.6
9.8, 5.0
0
.5
1.0
0
.5
1.0
TIME (sec)

Figure 11

the left of the midline at the occiput. In fact, the regions of strongest response were temporal and occipital, while intervening areas gave either weak responses or no detectable responses at all. These results are qualitatively quite similar to those reported by Okada et al. (1983) obtained using gratings as stimuli.

Isofield contours were plotted to show how the field measured when 'P300' was at its peak varied as a function of position about the scalp (Figure 12). The important thing to note is that the field extrema in the occipital region are not well defined. This is attributable to overlap of fields of opposite directions. However, the location of the extremum to the right of the midline can estimated by interpolation. It lies between the two positive "apparent" extrema. These are probably produced by the overlapping negativity (inwardly directed field) associated with the source whose field emerges from the left temporal region and reenters in the occipital region. The corresponding extremum over the right temporal region is much more clearly defined.

Using the locations of the estimated occipital extremum and the extremum over the right temporal region as reference points, we made use of the sphere model to estimate the location of the source giving rise to these two extrema. This estimation is shown in Figure 13. Despite the evident "noisiness" in these



P3
Vertical distance along midline (cm)
Horizontal distance from inion (cm)
Distance from ear (cm)

Figure 12

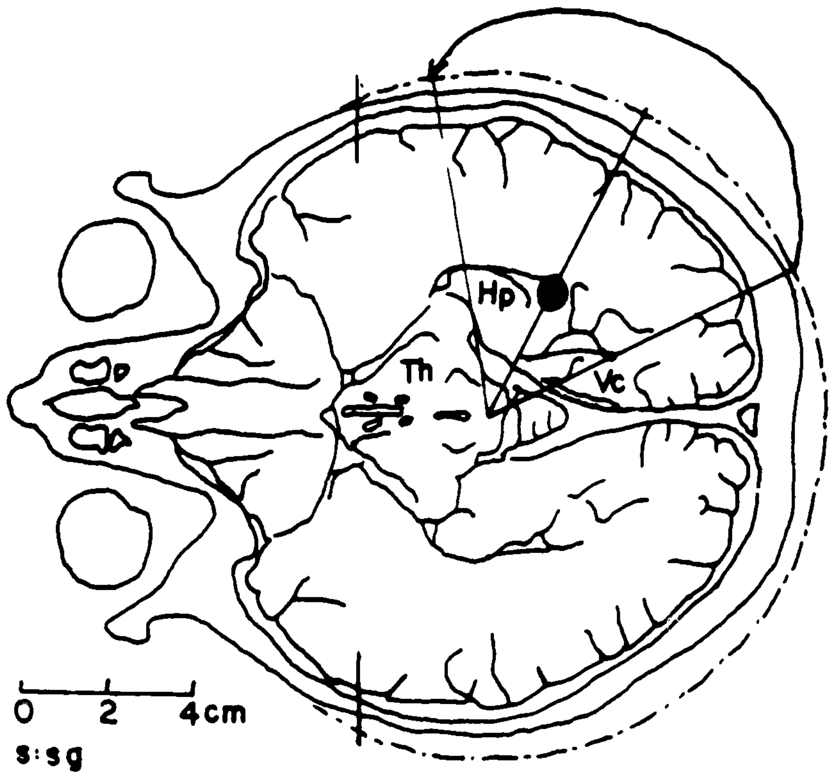


Figure 13

data, it is obvious that we are dealing with a very deep (subcortical) source. Also, the equivalent current dipole source appears to be located within 1 cm of the position of the source in the experiment using grating stimuli. This places the source in or near the hippocampal formation, as concluded previously. It should be stressed that this consistency in source location is present despite the fact that alphanumeric stimuli were employed in this experiment, while grating stimuli were employed in the earlier experiment.

It is worth noting that students of the limbic system are unclear about the precise boundaries of the so-called hippocampal formation. It is not a well defined anatomical entity. Even so, our results are consistent with the previous results, at least within our experimental error, and as Halgren and his colleagues (1980) have pointed out, strongly implicate the limbic system.

The preceding experiment was conducted to determine if alphanumeric stimuli employed in the McCarthy and Donchin experiment can be used effectively to conduct magnetic P300 studies. An important criterion is whether or not the signal-to-noise ratio is adequate. This seems to be true for fields measured in the temporal regions. However, occipital field patterns are somewhat confusing because of the partial overlap of fields of opposite polarity. It is possible to surmount this

diffifficulty simply by choosing subjects who have large head diameters, as our experience has shown that the overlap of fields of opposite polarity in the occipital region is less when the head diameter is large. However, we now know that it is possible to locate an equivalent current dipole source by measuring the field near only one extremum (see Section 4.0 on Neural Source Location with Minimal Data). We shall use this procedure in a new experiment designed to determine if experimental manipulations that result in significant changes in the electrical P300 result in a change in the position or orientation of the underlying equivalent current dipole source. This new experiment will be described in Section 5.0 below.

4.0 Neural Source Location with Minimal Data:

The procedure and analysis described here was carried out in collaboration with Professor Paulo Costa Ribeiro, of the Pontificia Universidade Catolica, Rio de Janeiro, Brasil, who served as a Guggenheim Fellow in our laboratory for a period of five months.

When our five channel neuromagnetometer (Freddy) was placed into operation, there was only one other multi-channel system in operation. This was the 4-sensor system used in the shielded room at the Helsinki University of Technology. Since then, another 4-sensor system was installed by the Laboratory for Solid State Electronics of the CNR in Rome at a site remote from

urban magnetic noise. There is a fundamental difference in the capabilities of these instruments. Aside from Freddy being useable in a noisy environment, it is the only system capable in principle of determining the position and strength of a neural source (modelled as an equivalent current dipole) without having to actually move the dewar. This is because a current dipole is characterized by five parameters (three for position, one for strength, and one for the angular orientation of the dipole moment in the plane tangential to the scalp), and therefore only five measurements of the field are needed to locate a neural source. Thus, in low-noise situations, we do not have to move the dewar to monitor all of the relevant parameters describing a current dipole source. We call such a procedure the "single position method."

The advantages of single-position localization are obvious: change in position, orientation or strength of the source can be monitored as the stimulus or the task is altered. Also, we avoid the innaccuacies associated with moving a dewar from position to position since the source may change as a result of time (due to habituation, for example) during sequential measurements. Parallel measurements with five channels avoids the assumption of stationarity, and fewer sequential measurements minimize effects of departures from stationarity.

However, another requirement must also be met to effectively exploit this potential advantage of our 5-sensor system: the relative electronic gains of the five signal channels must be established with high precision. Otherwise, appreciable systematic errors will be introduced in locating sources. The conventional procedure of calibrating the ratio of voltage output per femtotesla of applied field is to place a small field coil directly under the detection coil of a given channel, and observe the output voltage for a given current through the field coil. From a calculation of the mutual inductance between the field coil and detection coil, the net magnetic flux produced in the latter can be deduced, and from that the equivalent applied field at the pickup coil. However, the observed voltage is <u>extremely</u> sensitive to exactly where the field coil is placed, causing a resulting uncertainty of about 10% in the calibration of each channel. This is too great for determining the position within the head of a neural source with the sngle-position method, and consequently another procedure was conceived and developed.

We exploited the fact that the detection coil of each signal channel is wound as a second-order gradiometer and is very well balanced in the product of area-turns for the different coils so as not to respond to a uniform field. The balance is about 1 part in 100,000. We realized that if we use a

large field coil, say a square coil about 2.5 meters on a side, to produce a field along the axis of the detection coil, the channel will not respond to the uniform field produced by the coil (the response will only be 10 ppm of the applied field). It will only respond to the spatial second derivative of the field along the axis. (There is no first derivative if the field is centered on the detection coil). The value of this second derivative can be accurately calculated for a given current passing through the field coil, and it is found to be 100 times greater than the residual 10 ppm pickup of the uniform field. Thus, by observing the corresponding voltage output of the chanel we obtain an accurate calibration of the ratio of voltage output per femtotesla of equivalent field.

This procedure was carried out and very reasonable values were obtained for each signal channel. Thus the relative gains of the channels are established with a precision of about 2%, which is entirely adequate for single-position localization of neural sources. The method is being applied experimentally in studies of auditory evoked responses.

Computations are presently underway to establish how the accuracy of locating sources is affected by various levels of field noise. Initial results indicate that a noise level that is 10% of the maximum signal is tolerable in terms of present standards of accuracy. An abstract of a talk to be presented at

the forthcoming meeting of the American Physical Society is provided as part of this Section, and a long manuscript is in preparation for publication.

5.0 Planned P300 Experiment:

Since developing the single-position method, we came to the conclusion that this would provide the best means for completing the P300 investigation described in Section 3.0. It was apparent that we had difficulties in determining the precise positions of the occipital extrema. However, by positioning the dewar over one temporal extremum and measuring the field at five positions at once, we could use the single-position method to determine if the position of the source of P300 changes when experimental consditions cause the amplitude and latency of P300 to change. Toward this end, we now have a program that will allow us to present both auditory and visual stimuli, where either can serve as the odd-ball stimulus. The P300 to the visual odd-ball differs in latency from the auditory. Our first test will be to see if there is a difference in the fields across the five positions when the latency of the P300 changes. As a next step, repeated measures will minimize the effects of noise, so that we should be able to deduce the location(s) of the source(s) of P300. This work will be underway in April of 1986, and if it turns out to be promising, we will then implement the original paradigm of McCarthy and Donchin.

6.0 Project Haystack:

We conclude this scientific report with a brief account of work that was not done in connection with this project. However, it provides us with our first objective measure of the precision with which we can locate sources of magnetic fields within the human body.

We were approached by a man (whom we shall call Mr. Haystack to preserve his anonymity) who had been suffering with tinnitus. All previous medical treatments had failed, so he sought help from an acupuncturist. Unfortunately, during the course of treatment a 1/2 inch length of the acupuncture needle broke off in Mr. Haystack's back. The gauge 32 needle was very thin, and appeared in only one of 30 X-rays taken at various times. Surgery was performed twice before we saw Mr. Haystack, and the surgeons were convinced that the needle was gone, even though they had not seen it. However, Mr. Haystack complained of sticking pains, and was afraid that the needle was migrating. He approached us because a physicist told him that our neuromagnetometer might have sufficient sensitivity to detect it.

Although the needle was nominally made of stainless steel, when we placed the neuromagnetometer over Mr. Haystack's back and moved him under it, it was clear that magnetic material was present. We mapped this magnetic field and found that it could

be modelled by a magnetic dipole. Moreover, using algorithms similar to those we employed on this AFOSR project, we deduced a position, depth and orientation of the needle. After consultations with the physician supervising Mr. Haystack's evaluation, a surgeon at NYU was asked to review the case. He requested a CT scan where the "slice" would be directly through the site at which we deduced the needle would be found. Using special high-resolution film a dot was found within 3 mm of where we placed the needle. (Actually, we placed the needle at a depth of 2.8 cm in the intercostal space between two ribs and located it laterally relative to protuberances of the spine and the scapula). Surgery was then performed, and the needle was found with ease. The surgeon determined its approximate depth to be 2.5 cm. Evaluation of the CT scan will give us a more precise measure.(It should be noted that prior to working on Mr. Haystack we conducted double blind trials with a small needle hidden beneath fabric and imbedded in foam rubber. We mapped the field patterns here and determined the position and orientation of the needle. These determinations were compared with the actual position of the needle which was measured after the fact. Again, accuracy was better than 3 mm.)

A report describing the foregoing project is being written for publication. Its authors are R. Ilmoniemi, S. J. Williamson, L. Kaufman and H. Weinberg M.D.

ADDENDUM

Annual Report: Perceptual Factors in Workload: A Neuromagnetic Study
AFOSR Contract F49620-85-K-0004
01/01/85 - 12/31/85

PERSONNEL

Lloyd Kaufman
Professor of Psychology
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Yoshio Okada
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Visiting Research Scientist

David Shakun
Graduate Research Assistant

Carley Paulsen
Graduate Research Assistant

William Salem
Secretary/Office Manager

PRESENTATIONS

Invited Talks:

7 January	"The Physics and Instrumentation of Magnetic Field Recording", Seventh Annual Carmel Conference on Cognitive Psychology. Carmel, California, January 6-11, 1985.
14 March	"Neuromagnetism: A New Frontier in Brain Research", IEEE Society on Magnetics Regional Meeting, Pittsburgh, Pennsylvania.
22 March	"Neuromagnetism: A New Frontier in Brain Research", Colloquium, Department of Physics and University Chapter of Sigma Xi, University of Connecticut, Storrs, Connecticut.
3 April	"Neuromagnetism: A New Frontier in Brain Research", Colloquium, Department of Physics, Duke University, Durham, North Carolina.
15 May	"Magnetic Fields of the Human Brain", Colloquium, Department of Physics, University of Minnesota, Minneapolis, Minnesota.
20 May	"Neuromagnetism: A New Frontier in Brain Research", Engineering and Science Colloquium, NASA Goddard Science Center, Greenbelt, Maryland.
19 November	"Determining Sources in the Brain from Neuromagnetic Studies: An Ill-posed Problem", Seminar on Mathematical Biology, Courant Institute of Mathematical Sciences, New York University.
12 December	Colloquium, Department of Psychology, Harvard University.
27 October	Workshop on Military Standards for Vision and Hearing, Washington DC, National Research Council
August 1985	XIV International Conference on Medical and Biological Engineering VII International Conference on Medical Physics (both conferences in Espoo, Finland) 11th International Congress of EEG and Clinical Neurophysiology in London, England Papers presented at each of the above conferences.
March 1985	Principal Organizer for Conference held by "Columbian Association of Neurobiology" in Bogata, Columbia.

ADDENDUM (Continued)

PROFESSIONAL ACTIVITIES

Samuel J. Williamson

- Consultant, Los Alamos Scientific Laboratory, Life Sciences Division
- Member of National Institutes of Health Special Study Sections
- Chairman of the North and South American Program Committee for the International Biomagnetism Conference to be held in Tokyo in August, 1987
- Awarded Doctor of Science, honoris causa, by New Jersey Institute of Technology, May 23, 1985.

Lloyd Kaufman

- Member of the NAS-NRL Committee on Vision 1983-85
- Fellow American Psychological Association
- Fellow AAAS
- Member Society of Experimental Psychologists
- Member ARVO
- Member Board of Directors, New York Association of the Blind

WORK IN PROGRESS OR SUBMITTED FOR PUBLICATION

"Neuromagnetic Imaging: Viewing the Mechanics of Thought"
L. Kaufman and S.J. Williamson in "The NYU Physician", Fall 1985, pp 38-41, in "University", December 1985.

"Analysis of Neuromagnetic Signals"
S.J. Williamson and L. Kaufman invited for "Handbook of Electroencephalography and Clinical Neurophysiology," A. Givens and A. Remond, Eds. (Elsevier, Amsterdam), in press.

"Magnetic Localization of a Foreign Body"
R.J. Ilmoniemi, S.J. Williamson, L. Kaufman and H. Weinberg in preparation, to be submitted to New England Journal of Medicine.

"Neural Source Localization with Minimal Magnetic Data"
C. Costa Ribeiro, S.J. Williamson and L. Kaufman in preparation, to be submitted to Journal of Applied Physics.

ABSTRACT FOR A TALK TO BE GIVEN AT THE
MEETING OF THE AMERICAN PHYSICAL SOCIETY
31 MARCH - 4 APRIL 1986

Equivalent Dipole Source Determination With Minimal Neuromagnetic Data.* P. Costa Ribeiro+, S.J. Williamson, and L. Kaufman, New York University-- We have demonstrated the feasibility in certain situations of completely characterizing localized neural activity in the human brain by measurements with a five-sensor neuromagnetometer[1] placed at an appropriate location over the scalp. When a good signal-to-noise ratio can be obtained it is thereby feasible to follow amplitude, orientation, or position changes of a nearby neural source without having to take sequential measurements at a large number of locations. However, when the signal-to-noise ratio falls appreciably below 10 the precision in source determination decreases markedly. Computer simulations will be compared with actual measurements of magnetic fields evoked by auditory stimuli.

*Supported in part by NIH Grant NS-19463-01, ONR Contract N00014-85-K-0036, and AFOSR Grant F49620-85-K-0014.

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1. S.J. Williamson, M. Pelizzone, Y. Okada, L. Kaufman, D.B. Crum, and J.R. Marsden, in Proc. Tenth Intl Cryogenic Engineering Conference, H. Collan, P. Berglund, and M. Krusius, Eds. (Butterworth, Guildford, England, 1984), pp 339-348.

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